

REMARKS

The Examiner reasserts an obviousness rejection as summarized below.

- I. Claims 1-3 are rejected under 35 USC § 103(a) as allegedly unpatentable over *United States Patent Application Publication No. 2002/0147196 To Quessy et al.*, in view of Zakrzewska et al. *J. Neurol Neurosurg Psychiat* 52:472-476 (1989).

The Examiner is requested to note that the Applicants have voluntarily inserted a “comma” into Claim 1 in order to improve clarity.

I. Claims 1-3 Are Not Obvious

The legal standard for determining a *prima facie* case of obviousness has recently been reaffirmed as consisting of three elements where:

... the scope and content of the prior art are to be determined ... [the] differences between the prior art and the claims at issue are to be ascertained; and the level of ordinary skill in the pertinent art resolved. Against this background the obviousness or nonobviousness of the subject matter is determined.

KSR v. Telflex pg 2, Slip Op. (S. Ct. May 2007) (hereinafter referred to as *Teleflex*). In the present case the Examiner has not fulfilled the burden of addressing any of these elements. Instead, the Examiner has cobbled together unrelated teachings from two references in a strained attempt to form an obviousness rejection. Further, the Examiner has made numerous conclusory statements without providing any articulated reasons having a rational underpinning.¹ The Applicants incorporate by reference the arguments made against this same rejection in the last Office Action response and respectfully request reconsideration by the Examiner.

¹ *In re Kahn*, 441 F. 3d 977, 988 (CA Fed. 2006) (“[R]ejections on obviousness grounds cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness”) *cited in Teleflex at pg 14*.

A. Quessy et al. And Zakrzewska et al. Do Not Provide Any Articulated Reasons For A Combination

The Examiner states that the Applicants' previous response is not persuasive because:

... the strongest rationale for combining references is ... a convincing line of reasoning based on established scientific principles or legal precedent, that some advantage or expected beneficial result would have been produced by their combination.

Office Action, pg. 2 –3. The Applicants disagree. The Examiner must realize that Quessy et al. simply lists oxcarbazepine as one of five possible sodium channel blockers. *Quessy et al.*, para [0011]. Quessy et al. provides no information showing that combinations of bupropion with either oxcarbazepine or lamotrigine have similar therapeutic benefits.

The Examiner is reminded that the presently claimed embodiment encompasses a formulation comprising a drug combination. The Examiner has not shown that Zakrzewska et al. suggests any desirability to provide any drug combination. In fact, the Applicants have failed to find that Zakrzewska et al. even mentions a drug combination in any context. Consequently, Zakrzewska et al. provides no motivation or suggestion that oxcarbazepine could, or should, be combined with any drug, must less bupropion. This fact provides a helpful insight² into the fact that the Zakrzewska et al. and Quessy et al. reference combination is improper.

Consequently, the Applicants conclude that Zakrzewska's teachings cannot be properly combined with Quessy's teachings and respectfully request that the Examiner withdraw this rejection.

B. The Suffin Declaration

The Applicants point to the attached 35 USC 132 Declaration by the lead inventor, Dr. Steven Suffin (herein after, "The Suffin Declaration"). The Suffin Declaration meets the recent Supreme Court holding that showing "unpredictability" over the art is sufficient to remove an obviousness rejection:

²*KSR v. Teleflex*, pg 14.

The combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results.

and,

The fact that the elements worked together in an unexpected and fruitful manner supported the conclusion that Adam's design was not obvious to those skilled in the art.

KSR v Teleflex, Slip Op., pg. 12 (2007). The Applicants argue that The Suffin Declaration provides sufficient evidence to show that oxcarbazepine and lamotrigine does not work as expected by one having ordinary skill in the art. *Teleflex* teaches that the Examiner "... must ask whether the improvement is more than the predictable use of prior art elements according to their established functions". *KSR v. Teleflex, pg. 13*. The Applicants submit that although Quessy et al. teaches that both oxcarbazepine and lamotrigine are both sodium channel inhibitors, the Applicants provide evidence showing that these two drugs do not have similar effects on rEEG multivariable measurements.

The Suffin Declaration presents data showing that oxcarbazepine and lamotrigine have many electrophysiological differences in the qualitative and quantitative effects on rEEG multivariable measurements. In fact, fifty percent of the rEEG multivariable measurements had opposite responses to oxcarbazepine versus lamotrigine. When factoring in the quantitative differences between rEEG multivariable responses, sixty-seven of the rEEG multivariable responses demonstrated significantly different responses when comparing oxcarbazepine and lamotrigine. *Suffin Declaration para 4*.

These data clearly show that lamotrigine and oxcarbazepine cannot be assumed to be interchangeable. The Suffin Declaration also provides data showing that oxcarbazepine has an overall rEEG response pattern that is consistent with stimulant drugs. On the contrary, lamotrigine has an overall rEEG response pattern that is consistent with depressant drugs. *The Suffin Declaration para 5*.

B. Quessy et al. And Zakrzewska et al. Do Not Teach A Reasonable Expectation Of Success

The Examiner admits that Quessy et al. does not expressly teach a composition comprising a combination of oxcarbazepine and bupropion. *Office Action pg. 6*. Further, Quessy's brief mention of oxcarbazepine as a possible candidate for a drug combination

would be considered by the Supreme Court as failing the “obvious to try” test, thereby providing insufficient support for an obviousness rejection:

When there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show that it was obvious under § 103.

KSR v. Teleflex, pg 17. In this case, Quessy et al. does not meet the Supreme Court’s test that known options are “obvious to try” because there is no showing of “anticipated success”. The Suffin Declaration clearly shows the opposite rEEG characteristics of oxcarbazepine and lamotrigine which would not be expected to show successful similar response when combined with bupropion.

Consequently, the Applicants have shown that Quessy et al. and Zakrzewska et al. do not teach reasonable a expectation of success and respectfully request that the Examiner withdraw this rejection.

CONCLUSION

The Applicants believe that the arguments and claim amendments set forth above traverse the Examiner's rejections and, therefore, request that all grounds for rejection be withdrawn for the reasons set above. Should the Examiner believe that a telephone interview would aid in the prosecution of this application, the Applicants encourage the Examiner to call the undersigned collect at 617.984.0616.

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